

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:

Marcu et al.

Application No. Unassigned

Filed: September 12, 2001

Art Unit: Unassigned

Examiner: Unassigned

For: METHOD OF INHIBITING A  
CHAPERONE PROTEIN

**AMENDMENTS TO CLAIMS MADE VIA PRELIMINARY AMENDMENT**

*Amendments to existing claims:*

14. (Amended) The method of [any of claims 1-13] claim 1, wherein the chaperone protein is in a cell and cellular proliferation is inhibited.

16. (Amended) The method of [any of claims 1, 3-6, 12, and 13] claim 1, wherein the client protein is hepatitis B virus reverse transcriptase.

18. (Amended) The method of [any of claims 1, 3-6, 12 and 13] claim 1, wherein the client protein is a steroid hormone receptor.

20. (Amended) The method of [any of claims 1, 3-6, 12 and 13] claim 1, wherein the client protein is in a cell and is Hsf-1.

22. (Amended) The method of [any of claims 1-21] claim 1, which is *in vivo*.

23. (Amended) The method of [any of claims 1-21] claim 1, which is *ex vivo*.

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**PENDING CLAIMS AFTER ENTRY OF PRELIMINARY AMENDMENT**

1. A method of inhibiting binding of a chaperone protein with its client protein or client polypeptide, wherein the method comprises contacting a chaperone protein with coumarin or a coumarin derivative, such that the coumarin or the coumarin derivative binds the chaperone protein, which binding inhibits the chaperone protein from binding its client protein or client polypeptide.
2. The method of claim 1, wherein the chaperone protein is heat shock protein (Hsp) 90.
3. The method of claim 1, wherein the coumarin or coumarin derivative is a coumarin antibiotic.
4. The method of claim 3, wherein the coumarin antibiotic is chlorobiocin or coumermycin A1.
5. The method of claim 3, wherein the coumarin antibiotic is novobiocin.
6. The method of claim 2, wherein the coumarin or coumarin derivative is novobiocin.
7. The method of claim 6, wherein novobiocin binds a carboxyl-terminal region of Hsp90.
8. The method of claim 1, wherein the client protein or the client polypeptide is a tyrosine or serine/threonine kinase.

9. The method of claim 8, wherein the client protein or the client polypeptide is tyrosine kinase p185<sup>erbB2</sup> or p60<sup>v-src</sup>.

10. The method of claim 8, wherein the client protein or the client polypeptide is serine/threonine kinase Raf-1.

11. The method of claim 1, wherein the client protein or the client polypeptide is a mutated p53 protein.

12. The method of claim 1, wherein the client protein or the client polypeptide is inactive subsequent to binding of the chaperone protein to the coumarin or the coumarin derivative.

13. The method of claim 12, wherein the client protein or the client polypeptide is degraded.

14. The method of claim 1, wherein the chaperone protein is in a cell and cellular proliferation is inhibited.

15. The method of claim 14, wherein the cellular proliferation is cancer.

16. The method of claim 1, wherein the client protein is hepatitis B virus reverse transcriptase.

17. The method of claim 16, whereupon hepatitis B virus is inhibited.

18. The method of claim 1, wherein the client protein is a steroid hormone receptor.

19. The method of claim 18, wherein the effect of the steroid hormone receptor is modulated.

20. The method of claim 1, wherein the client protein is in a cell and is Hsf-1.

21. The method of claim 20, wherein the response of Hsf-1 to stress is inhibited.

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22. The method of claim 1, which is *in vivo*.
  23. The method of claim 1, which is *ex vivo*.

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